

CLAIMS

WE CLAIM:

1. A method of synthesis of a nitro naphthalimide comprising:
combining 3-nitro-1,8-naphthalic anhydride and an aliphatic diamine in an organic solvent to form a solution; and
refluxing said solution.
2. A method of synthesis of mitonafide comprising:
combining 3-nitro-1,8-naphthalic anhydride and N,N-dimethylethylenediamine in an organic solvent to form a solution; and
refluxing said solution.
3. A method of synthesis of an amonafide analog comprising combining a mitonafide analog comprising a 3-nitro group, ammonium formate, and a catalyst in an organic solvent to reduce said 3-nitro group.
4. A method of synthesis of amonafide comprising combining mitonafide, ammonium formate, and a catalyst in an organic solvent.
5. A method of synthesis of a naphthalimide diammonium salt comprising:
dissolving a naphthalimide in an organic solvent; and
contacting said dissolved naphthalimide with an inorganic or organic acid to form a naphthalimide diammonium salt.
6. The method of Claim 5 wherein said inorganic acid is selected from the group consisting of hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid and phosphoric acid.
7. The method of Claim 5 wherein said organic acid is selected from the group consisting of acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malic acid, malonic acid, succinic acid, hydroxy succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid and salicylic acid.

8. A composition comprising a naphthalimide as a diammonium salt.
9. A composition according to claim 8 wherein the naphthalimide comprises amonafide as a diammonium salt formed by combining amonafide with an inorganic or organic acid.
10. A composition of Claim 9 wherein said inorganic acid is selected from the group consisting of hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid and phosphoric acid.
11. A composition of Claim 9 wherein said organic acid is selected from the group consisting of acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malic acid, malonic acid, succinic acid, hydroxy succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid and salicylic acid.
12. A composition according to claim 8 wherein said diammonium salt is amonafide dimesylate.
13. A composition according to claim 8 wherein said diammonium salt is amonafide dihydrochloride.
14. A composition comprising a substituted 3-amino-naphthalimide salt.
15. An aqueous solution consisting essentially of a dissolved amonafide diammonium salt, said solution being suitable for administration by injection, said solution comprising amonafide at between 1 and 250 mg/mL, said solution having a pH between 4.0 and 7.0.
16. An aqueous solution of amonafide according to claim 15 suitable for parenteral, intramuscular, subcutaneous, intravenous, intraperitoneal or intratumoral administration.
17. An aqueous solution of amonafide, said solution being suitable for administration by injection, said solution comprising amonafide at between 10 and 100 mg/mL, and said solution having a pH between 5.5 and 6.5.

18. The solution according to claim 17, wherein said solution is substantially free of sugars.
19. The solution according to claim 17, wherein said solution further comprises a pharmaceutically acceptable carrier.
20. The solution according to claim 19, wherein said carrier is provided at a concentration between about 0.1 to 100 mg/mL.
21. The solution according to claim 17, wherein said solution is provided in a unit dosage form.
22. A method for manufacturing a sterile pharmaceutical composition comprising a naphthalimide diammonium salt suitable for administration to a human, said method comprising:
- (a) solubilizing a naphthalimide diammonium salt in an aqueous solution;
 - (b) neutralizing the aqueous solution with a molar equivalent of base;
 - (c) adjusting the pH of the solution comprising said solubilized naphthalimide diammonium salt to about 6; and
 - (d) sterilizing said solution.